









## CLINICAL ARTICLE

# Surgical Management for Chronic Destructive Septic Hip Arthritis: Debridement, Antibiotics, and Single-Stage Replacement is as Effective as Two-Stage Arthroplasty

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**Objective:** To compare the surgical outcomes of debridement, antibiotics, and single-stage total hip replacement (DASR) vs two-stage arthroplasty (two-stage arthroplasty) for chronic destructive septic hip arthritis (SHA).

**Methods:** Cases of chronic destructive SHA treated by DASR or two-stage arthroplasty in our department from January 2008 to October 2021 were retrospectively reviewed. Patient demographic information, perioperative inflammation markers, intraoperative blood loss, microbial culture, and metagenomic new generation sequencing results were recorded. The perioperative complications, hospital stay, hospitalization cost, infection recurrence rate, and Harris Hip Score (HHS) at the last follow-up were compared between the two groups.

**Results:** A total of 28 patients were included in the study, including 11 patients who received DASR and 17 patients who received two-stage arthroplasty. There was no significant difference in demographic information, preoperative serum inflammatory markers, synovial fluid white blood cell count, or percentage of polymorphonuclear leukocytes between the two groups. The DASR group demonstrated significantly lower intraoperative blood loss [(368.2 ± 253.3) mL vs (638.2 ± 170.0) mL,  $p = 0.002$ ], hospital stay [(22.6 ± 8.1) days vs (43.5 ± 13.2) days,  $p < 0.0001$ ], and hospitalization expenses [(81,269 ± 11,496) RMB vs (137,524 ± 25,516) RMB,  $p < 0.0001$ ] than the two-stage arthroplasty group. In the DASR group, one patient had dislocation as a complication. There were no cases with recurrence of infection. In the two-stage arthroplasty group, there was one case complicated with spacer fracture, one case with spacer dislocation, and one case with deep vein thrombosis of the lower limbs. There were no cases with recurrence of infection. There were no significant differences in the readmission rate, complication rate, or HHS at the last follow-up between the two groups.

**Conclusions:** Both DASR and two-stage arthroplasty achieved a satisfactory infection cure rate and functional recovery for chronic destructive SHA, and DASR demonstrated significantly lower intraoperative blood loss, hospital stay, and hospitalization costs than two-stage arthroplasty. For appropriately indicated patients, if microbial data are available and a standardized debridement protocol is strictly followed, DASR can be a treatment option.

**Key words:** Debridement; Next generation sequencing; Septic arthritis; Total hip arthroplasty

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## Introduction

Septic hip arthritis (SHA) is a relatively rare but extremely harmful disease in the population. If not diagnosed and treated in time, it can evolve to a chronic persistent state and quickly lead to progressive cartilage and bone destruction, eventually leading to loss of function<sup>1</sup>. The yearly incidence of SHA is estimated to be approximately 4–10 per 100,000 patients worldwide; however, its real incidence is difficult to quantify. SHA includes primary infection of the native joint and secondary infection after hip surgery. Primary SHA often originates from bloodstream dissemination from infections in other parts of the body. Infections secondary to a hip procedure or surgery, such as aspiration, arthrotomy, internal fixation for fractures, removal of internal fixations, etc., but not including periprosthetic joint infection (PJI), are also common causes of SHA if they are not diagnosed and treated in a timely and accurate manner<sup>2</sup>.

The treatment of SHA is complicated, and its standard treatment is still under debate. Early or acute SHA can be treated with arthrotomy and drainage, arthroscopic debridement, or open debridement, followed by systemic antibiotics<sup>3</sup>. However, some patients whose symptoms have persisted for a long time at initial treatment have already had articular cartilage and bone destruction or osteomyelitis. The failure rate of single arthroscopic or open debridement in these patients is relatively high and may quickly develop into chronic SHA<sup>4,5</sup>. For these patients, “head and neck resection” (Girdlestone surgery) has usually been performed in the past<sup>6</sup>. However, this type of surgery often leads to short limbs, joint pain, and poor functional recovery, which seriously affects the patient’s quality of life<sup>7</sup>. Single-stage total hip arthroplasty (THA) has been used successfully for quiescent infection but has shown poor outcomes for the management of active chronic destructive SHA, with most of the literature published in the 20th century<sup>8,9</sup>. In the modern era, two-stage arthroplasty is more favorable for chronic destructive SHA. The surgery includes two stages. In the first stage, thorough debridement and excision of the damaged femoral head and neck is performed, together with the implantation of antibiotic-impregnated spacers or beads, followed by systemic antibiotic therapy. After clinical judgment of a controlled infection, a second-stage surgery is performed, and a new artificial joint is implanted. It has been reported that two-stage arthroplasty for chronic destructive SHA achieves a satisfactory infection eradication rate<sup>2,5,10–12</sup>. However, despite encouraging outcomes, this strategy requires at least two operations, which increases the hospital stay, costs, and anxiety level of patients. Spacer-related complications, such as dislocation or fracture, have also been reported in the literature<sup>13</sup>.

In recent years, many studies have reported that the use of debridement combined with single-stage revision achieves similar outcomes, with reduced morbidity and costs, compared to two-stage revision for chronic PJI<sup>14,15</sup>. Some researchers have also demonstrated the use of conversion THA, which includes irrigation and debridement (I&D) by

the open or arthroscopic method in the first stage, followed by elective arthroplasty in the second stage, which could achieve an 88.6% success rate for active SHA<sup>16</sup>. Based on these findings, we hypothesize that debridement and single-stage replacement followed by sensitive antibiotics could achieve a similar success rate and can be selectively indicated for patients with active chronic destructive SHA. This protocol would prevent patients from developing spacer-related complications, largely preserve bone mass, and reduce damage to soft tissues.

As a tertiary referral center for bone and joint infection, our institution has admitted dozens of cases of chronic destructive SHA. The purpose of this study is to (i) report the surgical outcomes for chronic destructive SHA in our institution; (ii) specifically compare the treatment success rate, complications, and follow-up results of debridement, antibiotics, and single-stage replacement (DASR) *vs* two-stage arthroplasty for chronic destructive SHA; and (iii) investigate whether DASR can be a treatment option for chronic destructive SHA and its indications.

## Methods

### Study Characteristics

This research protocol has been reviewed and approved by the ethics committee of our institution [(2015)084-1]. The cases of chronic active destructive SHA admitted to our department from January 2008 to October 2021 were retrospectively reviewed. Patient demographic information (age, sex, surgical side, if combined with sinus, past medical history, surgical history, time of symptoms to surgery) was traced and recorded.

### Inclusion and Exclusion Criteria

The inclusion criteria were as follows: (i) chronic destructive SHA patients with definite joint destruction and narrowing of the joint space on imaging studies with symptoms persisting for more than 3 weeks on admission; (ii) patients who received DASR or two-stage arthroplasty surgery; and (iii) patients who had completed records of clinical data and follow-up results.

Cases with the following conditions were excluded: (i) acute SHA with less than 3 weeks of symptoms and indefinite joint destruction and joint space narrowing; (ii) sequelae of SHA or quiescent SHA; (iii) tuberculosis of the hip; (iv) patients treated with other treatment options, including single antibiotic treatment, single open or arthroscopic debridement, or Girdlestone surgery; (v) the two-stage strategy was selected, but the second-stage surgery has not yet been performed; (vi) PJI after primary joint replacement; or (vii) follow-up of less than 1 year.

The diagnosis of SHA was based on the patient’s medical history, clinical manifestations, laboratory and imaging examinations, pathological examination, microbial culture, and new molecular diagnostic technology. The diagnosis was made by any of the following<sup>5</sup>: (1) gross purulence in the

joint; (2) positive preoperative inflammatory markers (an erythrocyte sedimentation rate (ESR) greater than 30 mm/h and C-reactive protein (CRP) level greater than 10 mg/L) and one or more of the following: (a) one or more positive intraoperative culture; (b) a positive culture from an aspiration; (c) positive frozen section at the time of insertion of the spacer (greater than five white blood cells [WBCs] per high-power field); and (d) an elevated synovial fluid white blood cell (WBC) count (greater than 3000).

The definition of treatment success was that the patient had no local infection-related symptoms at the last follow-up, with the inflammatory markers returned to normal, the imaging examination did not suggest signs of infection (such as prosthesis loosening, bone resorption, or osteolysis), and the surgeons judged that the infection had been eradicated. If the infection relapsed or required one or more operations, the treatment was considered to have failed. The diagnostic criteria of infection recurrence referred to the 2018 Musculoskeletal Infection Society (MSIS) guideline for PJI<sup>17</sup>.

### **Surgical Technique**

#### *Aspiration before Surgery*

Patients with highly suspected active SHA routinely underwent aspiration in a sterile environment before the operation under the guidance of ultrasound or CT scan if necessary. The aspirated synovial fluid or pus was immediately sent for WBC count and microbial culture, including bacteria (aerobic and anaerobic), fungi, and tuberculosis, as well as an antibiotic susceptibility test and metagenomic next-generation sequencing (mNGS) test. The culture duration was usually 5–7 days, but in special cases, it was extended to 14 days. In case of failed aspiration, a complete set of specimens was collected during the operation and transported immediately by designated personnel for further investigation.

#### *Selection of Surgical Strategy*

Generally, if the patient had a good nutritional status (with normal hemoglobin and albumin levels), no history of immune dysfunction or previous multiple operations, shorter duration of symptoms (generally less than 12 weeks), available microbiology data, and single surgery, we performed DASR. The availability of microorganism data is key. For patients with anemia or hypoalbuminemia, with a longer duration of symptoms (generally more than 12 weeks), accompanied by a variety of systemic diseases or with a history of multiple operations, with large bone defects or poor soft tissue conditions, with unavailable microbiology data or refractory microbiology, or who requested staged surgeries, two-stage arthroplasty was performed (Figure 1).

#### *Surgical Steps*

All operations were performed by the same experienced senior surgeon. The standard posterolateral approach was used. The skin and subcutaneous tissue were cut layer by layer to expose the hip joint capsule. The pus in the joint

cavity was aspirated before incision of the capsule and immediately sent for examination, including WBC and polymorphonuclear leukocyte (PMN) counts, microbial culture, susceptibility test, and mNGS test. For patients with internal fixation, the hardware was removed and sent for a sonication test. The sonication fluid was sent for microbial culture and mNGS. The hip joint was then fully exposed, and the damaged femoral head and neck were removed, followed by thorough debridement to remove purulent secretions, inflammatory granulation tissue, and scars if they existed. Three to five synovium or granulation tissues with the most obvious inflammatory lesions or inflammatory changes were cut with a scalpel and sent for intraoperative frozen section and pathology examinations, microbial culture, and mNGS if necessary. The surgical site was washed repeatedly with saline and hydrogen peroxide and soaked with iodophor-based solution. Surgical instruments, gloves, and gowns were replaced, and redraping was performed.

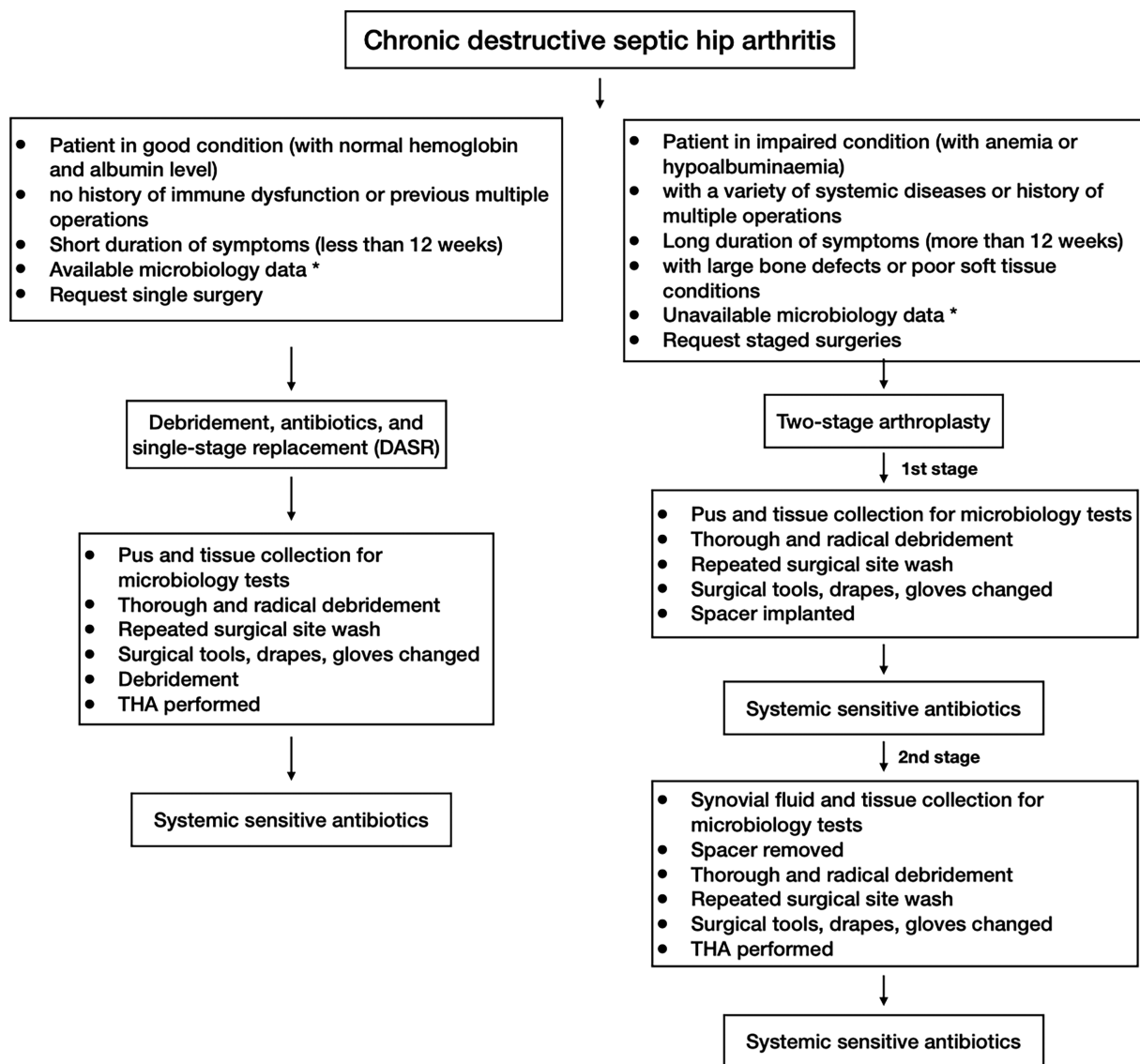
#### *Surgical Steps of DASR*

For patients who underwent DASR, meticulous debridement was performed again to remove remnant infective tissues. The acetabular and femoral prostheses were implanted successively according to the standard surgical manuals. Hip mobility was tested, and the surgical site was lavaged repeatedly. A drain was placed according to the intraoperative blood loss, and the incision was closed layer by layer. If a drain was placed, the tube was normally removed within 48 h. None of the patients received intra-articular antibiotic injection or lavage. After the operation, low molecular weight heparin (LMWH) was administered routinely, and rehabilitation was carried out under the guidance of physical therapists.

#### *Surgical Steps of Two-Stage Arthroplasty*

For patients who received two-stage arthroplasty, antibiotic-impregnated cement spacers were implanted. Antibiotics were impregnated into the bone cement according to the preoperative microbial results. Briefly, if it was gram-positive bacteria, 2 g vancomycin per 40 g bone cement (Zimmer Biomet) was prepared. If it was gram-negative bacteria, 1 g meropenem per 40 g bone cement was prepared. If the preoperative culture was negative or if culture results were unavailable, 2 g vancomycin and 1 g meropenem per 40 g bone cement were prepared. The spacers were all articulating spacers. After spacer implantation, the mobility of the hip joint was tested. The surgical site was washed repeatedly with saline. Joint cavity drainage was placed, and the incision was closed layer by layer. The drainage was normally removed within 48 h after surgery. None of the patients received intra-articular antibiotic injection or lavage. Routine anticoagulation with LMWH was administered, and rehabilitation was carried out under the guidance of physical therapists.

After systematic antibiotic treatment (including intravenous and oral administration, as described below) and clinical evaluation of the eradication of infection, second-stage revision surgery was performed. The criteria for judging controlled infection were as follows: (1) patient had no



**Fig. 1** Flow diagram of surgical selection for chronic destructive SHA in our institution. (\*: key indication).

infection-related symptoms (incision healed well with no sinus, no active or resting hip pain, no swelling of soft tissue, and normal body and skin temperature); (2) normal inflammatory marker levels (including WBC, CRP, and ESR levels); and (3) imaging examination did not indicate infection signs, such as bone resorption and osteolysis. The original surgical incision was used, the skin and subcutaneous tissues were cut layer by layer, and the wound was debrided again. The joint fluid and tissue samples were sent for frozen section examination, microbial culture and mNGS test if necessary. The spacer was removed, and the remaining cement was carefully removed. The incision was repeatedly lavaged with saline and hydrogen peroxide and soaked with iodophor-based solution. Surgical instruments, gloves, and gowns were replaced, and redraping was performed. The femoral stem and acetabular cavity were

reamed, and the total hip prosthesis was implanted. If necessary, a revision prosthesis, cage, or cable/wire was used if the bone defect was large. The incision was washed repeatedly with continuous pulse lavage. A drain was placed according to the intraoperative blood loss and was normally removed within 48 h. The incision was closed layer by layer. None of the patients received intra-articular antibiotic injection or lavage. Postoperative anticoagulation and rehabilitation were performed after the first-stage surgery.

#### **Antibiotic Selection and Treatment Duration**

Treatment with antibiotics was decided after consultation and discussion with infectious disease specialists. If there was no complicated systemic infection, the patient was not given antibiotic treatment before obtaining the fluid or tissue

samples. For patients who had been treated with antibiotics in other hospitals, antibiotics were stopped for at least 2 weeks before joint aspiration. Vancomycin combined with meropenem was empirically selected for anti-infection treatment before the results of the culture and susceptibility tests were available. After obtaining the bacteriology results, specific antibiotics were administered. For cases with negative culture results, vancomycin combined with meropenem was prescribed. The duration of intravenous and oral antibiotics depended on wound healing and the CRP and ESR levels. Based on the microbial culture and drug susceptibility results, the total duration of treatment was normally 6–12 weeks. For patients with two-stage arthroplasty, after the first-stage surgery, routine intravenous antibiotics were used for 2–6 weeks and then changed to sensitive and highly bioavailable oral antibiotics. The total treatment duration was normally 6–8 weeks. Antibiotics were routinely stopped for 2 weeks before the second-stage surgery. After the surgery, antibiotics were selected according to the previous pathogen until new culture results were available.

### **Indicators of Observation**

#### *Inflammatory Markers*

Once an infection was suspected, blood tests of inflammatory markers, including WBC count, CRP, ESR, interleukin 6 (IL-6), and procalcitonin (PCT), were ordered. The synovial fluid was sent for WBC (SF-WBC) counts and the percentage of PMNs, microbial culture and mNGS tests. The blood test results of the last follow-up were also recorded, including WBC, CRP, and ESR levels. All these tests were performed at the Department of Laboratory Medicine in our institution.

#### *Perioperative Indications*

The intraoperative blood loss, perioperative complications, hospital stay, hospitalization costs, and infection recurrence of patients were recorded. This information was referred to from the medical records. For the two-stage arthroplasty group, the intraoperative blood loss, hospital stay, and hospitalization costs were calculated as the sum of the values of the two hospitalizations.

#### *Harris Hip Score (HHS)*

The HHS is used to evaluate pre- and postoperative recovery of hip function in an adult population. The HHS score system mainly includes four aspects: pain, function, absence of deformity, and range of motion. The score standard has a maximum of 100 points (best possible outcome). A total score <70 is considered poor, 70–80 is fair, 80–90 is good, and 90–100 is excellent. The results of the last follow-up were also recorded.

#### **Statistical Analysis**

The continuous data are presented as the means  $\pm$  SDs, and binary data are presented as counts and percentages. An independent-samples *t*-test or Mann–Whitney *U*-test was

used for continuous values, and a chi-squared test or Fisher's exact test was used for dichotomized values according to the estimated cell size. The significance of the *p* value was set to  $p < 0.05$ . Statistical analyses were performed in GraphPad Prism software (GraphPad Software, Inc., V8.2.0).

### **Results**

#### **Demographic Information**

From January 2008 to October 2021, a total of 35 patients with chronic destructive SHA were treated in our department. Among them, five patients underwent Girdlestone surgery, and one patient was lost to follow-up. These patients were excluded. The remaining 28 patients were included in this study, including 11 patients who received DASR (Table S1) and 17 patients who received two-stage arthroplasty (Table S2). For the 11 patients who underwent DASR, 10 were cases of primary SHA, and one was a secondary infection after hip surgery (Case 7, removal of internal fixation for intertrochanteric fracture). One patient had undergone arthroscopic debridement in a local hospital (Case 4), and one patient had a sinus tract (Case 8). Of the 17 patients who underwent two-stage arthroplasty, 11 patients had primary SHA, and seven had secondary infections after hip surgery (two cases of postoperative infection from pelvic fracture, four cases of postoperative infection from removal of internal fixation for femoral neck fracture, and one case of postoperative infection from femoral head cored decompression). Three patients had undergone open or arthroscopic debridement surgeries in other hospitals (Cases 2, 3, and 14), and one patient had a sinus tract (Case 17). There was no significant difference between the DASR group and the two-stage arthroplasty group in terms of age, sex, comorbidities, history of surgery, or time from symptoms to surgery (Table 1).

#### **Intraoperative Findings**

For most patients, pus in the joint cavity was available and was aspirated and sent for further studies. In cases of a dry tap, tissues were cut for microbial tests. In patients receiving DASR, after debridement of the acetabular side, no severe bone defects were seen; thus, no special cup or surgical techniques were needed. In patients receiving two-stage arthroplasty, particular attention was given when inserting the spacers to avoid excessively tight adhesion of the cement to the bone. During the second stage, after removing the spacers and remnant bone cement, no severe bone defects were observed in either the acetabular or femoral sides, with no special prostheses, bone grafts, or augments inserted. For the DASR group, all patients were implanted with cementless prostheses. For the two-stage arthroplasty group, there were 16 cases implanted with cementless prostheses and one case with cemented prostheses. No cases were implanted with revision prostheses.

**Table 1** Statistical analysis of age, sex, surgical side, comorbidities, time of symptoms to surgery, preoperative level of inflammation markers, HHS score, intraoperative blood loss, length of hospital stay, and hospitalization cost between the debridement, antibiotics, and single-stage replacement (DASR) group and two-stage arthroplasty group

	Debridement, antibiotics, and single-stage replacement (DASR)	Two-stage arthroplasty	t/z value	p value
Number	11	17	N/A	N/A
Mean age	57.6 ± 17.0	54.5 ± 15.7	0.48	0.63
Sex				
Male	7	11	0.058	0.95
Female	4	6		
Side				
L	6	9	0.083	0.93
R	5	8		
Comorbidities				
Sinus	1	1	N/A	0.99
Hypertension	2	4	N/A	0.99
Diabetes mellitus	2	3	N/A	0.99
Hepatitis B	3	2	N/A	0.35
Renal impairment	1	1	N/A	0.99
Pneumonia	1	2	N/A	0.99
Inflammatory diseases	2	0	N/A	0.16
History of surgery	2	1	N/A	0.55
Time of symptoms to surgery (weeks)	17.0 ± 17.1	58.4 ± 97.4	1.39	0.18
Preoperative WBC ( $\times 10^9/L$ )	6.8 ± 2.2	8.6 ± 2.7	1.84	0.08
Preoperative CRP (mg/L)	33.5 ± 32.3	43.9 ± 36.9	0.76	0.45
Preoperative ESR (mm/h)	67.7 ± 27.1	66.2 ± 35.7	0.12	0.90
Preoperative IL-6 (pg/mL)	37.0 ± 18.1	32.8 ± 22.0	0.36	0.72
Preoperative PCT (ng/mL)	4.0 ± 10.6	0.03 ± 0.06	1.28	0.22
SF WBC ( $\times 10^9/L$ )	12,439 ± 15,105	35,412 ± 57,331	1.28	0.21
SF PMN (%)	87.2 ± 6.6	80.1 ± 9.1	2.06	0.053
Preoperative HHS score	46.2 ± 14.8	44.9 ± 14.9	0.22	0.83
Intraoperative blood loss (mL)	368.2 ± 253.3	638.2 ± 170.0	3.39	0.002
Length of Hospital stay (days)	22.6 ± 8.1	43.5 ± 13.2	4.69	<0.0001
Hospitalization cost (in RMB)	81,269 ± 11,496	137,524 ± 25,516	6.84	<0.0001

Abbreviations: HHS, Harris Hip Score; RMB, Renminbi.

### Inflammatory Markers, Perioperative Indications, and HHS

There was no significant difference between the DASR group and the two-stage arthroplasty group in terms of the preoperative CRP, ESR, WBC count, SF-WBC, percentage of PMNs, HHS, or other indicators (Table 1). However, the DASR group demonstrated significantly lower intraoperative blood loss [(368.2 ± 253.3) mL vs (638.2 ± 170.0) mL,  $t = 3.39$ ,  $p = 0.002$ ], hospital stay [(22.6 ± 8.1) days vs (43.5 ± 13.2) days,  $t = 4.69$ ,  $p < 0.0001$ ], and hospitalization costs [(81,269 ± 11,496) RMB vs (137,524 ± 25,516) RMB,  $t = 6.84$ ,  $p < 0.0001$ ] than the two-stage arthroplasty group.

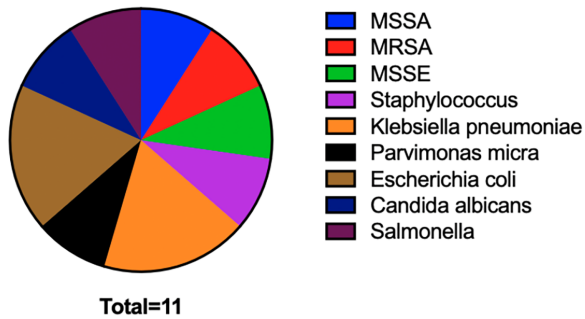
### Pathogens of Infection

The pathogens of infection are shown in Tables S1, Table S2, and Figure 2. For the DASR group, there was one case of methicillin-sensitive *S. aureus* (MSSA), one case of methicillin-resistant *S. aureus* (MRSA), one case of methicillin-sensitive *S. epidermidis* (MSSE), one case of *Staphylococcus*, two cases of *Klebsiella pneumoniae*, one case of *Parvimonas micra*, two cases

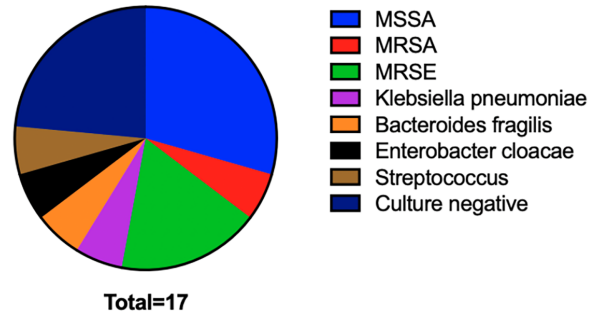
of *Escherichia coli*, one case of *Candida albicans*, and one case of *Salmonella*. The detection rate of pathogens was 100.0% (11/11). Six patients were tested with mNGS; five were positive, and one was negative. Among the five positive cases, four cases (Cases 3, 4, 5, and 6) showed results completely consistent with the cultures (*P. micra*, *E. coli*, *C. albicans* and *Salmonella*); one patient (Case 7) had a negative culture, but mNGS showed *Staphylococcus*. One patient (Case 1) was negative upon mNGS, while the tissue culture showed MRSA infection from a previous operation in another hospital. Antibiotics were used in this case for a long time before the operation. This was supposed to be the reason for the negative culture and mNGS in our hospital.

In the patients with two-stage arthroplasty, there were five cases of MSSA, one case of MRSA, three cases of MRSE, one case of *K. pneumoniae*, one case of *Bacteroides fragilis*, one case of *Enterobacter cloacae*, one case of *Streptococcus*, and four cases of negative culture. The detection rate of pathogens was 76.4% (13/17). Seven patients were tested with mNGS; five were positive and two were negative.

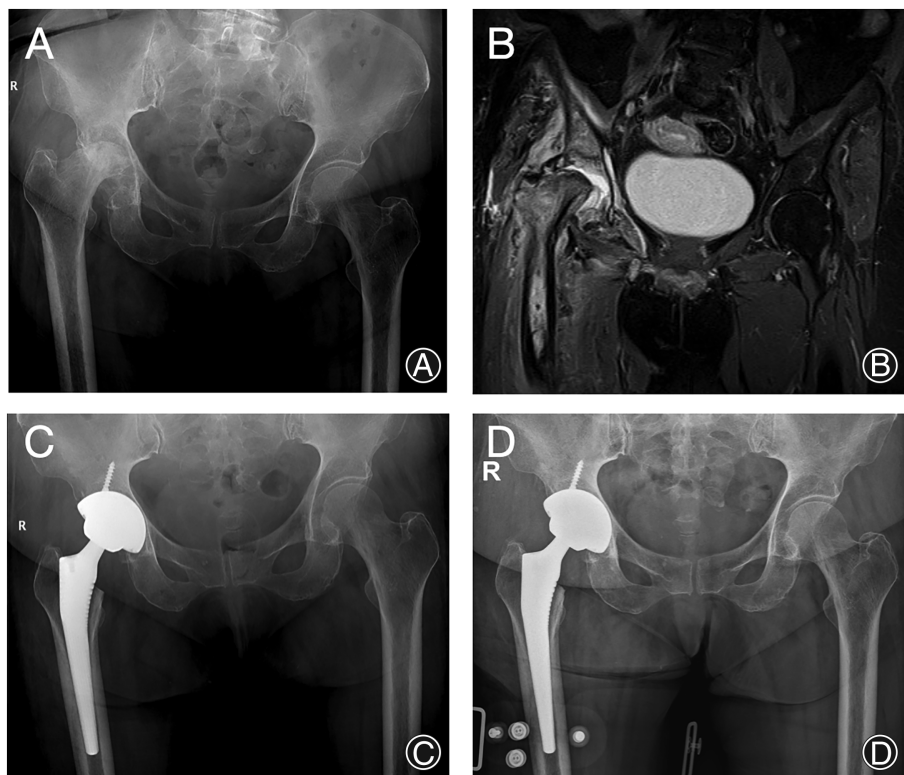
### Debridement, antibiotics, and single-stage replacement (DASR)



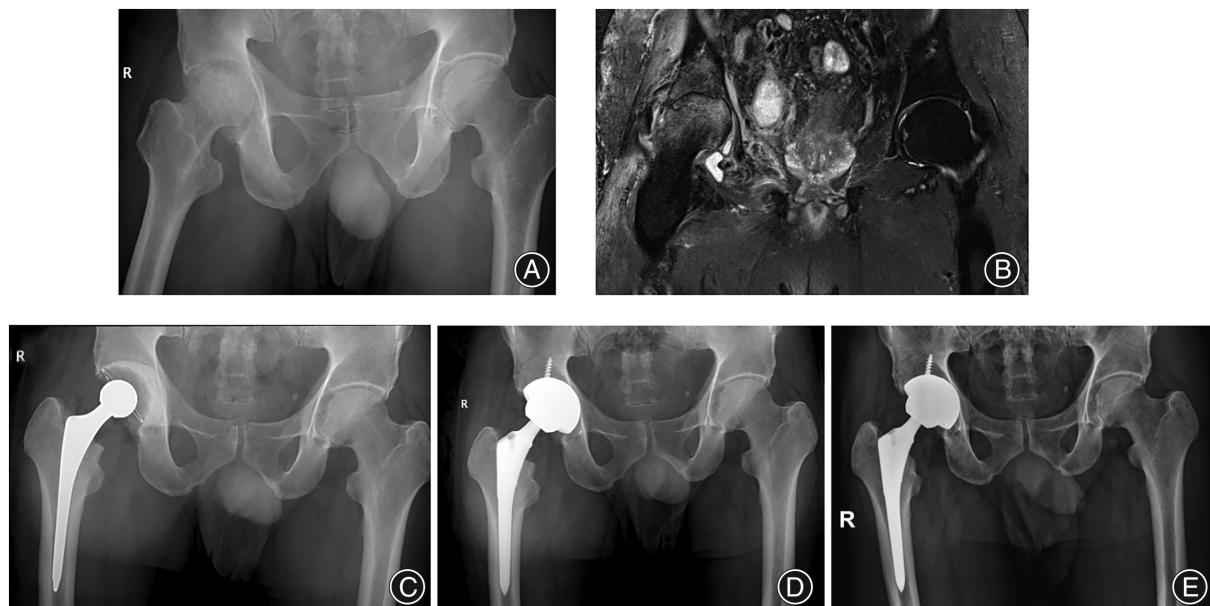
### Two-stage Exchange Arthroplasty



**Fig. 2** Pathogens of debridement, antibiotics, and the single-stage replacement (DASR) and two-stage arthroplasty groups.



**Fig. 3** A typical case (Case 3) of debridement, antibiotics, and single-stage replacement (DASR) for chronic destructive SHA. A 77-year-old female patient with a history of venous valve insufficiency of both lower limbs complained of repeated right hip pain for 1 year. Her preoperative CRP was 30.8 mg/L, and her ESR was 76 mm/h. (A) X-ray showed severe destruction of the superior aspect of the femoral head and adjacent acetabulum. (B) Magnetic resonance imaging (MRI) showed altered signal intensity in the right femoral head and neck and effusion. Aspiration was performed under the guidance of ultrasound before surgery, and the pus revealed WBC of  $3616 \times 10^6/L$  and PMN of 88%, with culture showing *Parvimonas micra*. (C) After discussion with the patient, the DASR strategy was selected. The tissue culture showed *P. micra*, which was consistent with the mNGS results. Empirical intravenous vancomycin and meropenem were administered, which was later changed to piperacillin tazobactam, for a total of 2 weeks, followed by oral amoxicillin for a total duration of 8 weeks. (D) The 23-month follow-up result showed satisfactory function of the right hip. Inflammatory markers were normal, and X-ray demonstrated a decent prosthesis position and no sign of infection.



**Fig. 4** A typical case (Case 4) of two-stage arthroplasty for chronic destructive SHA. A 59-year-old male patient with a history of diabetes and hypertension complained of recurrent right hip pain for 3 months. His preoperative CRP was 5.1 mg/L, and his ESR was 56 mm/h. (A) X-ray showed narrowing of the joint space and destruction of the left femoral head and acetabulum. (B) MRI revealed signal changes in the femoral head, with mild effusion. Aspiration was tried but failed to harvest pus under the guidance of ultrasound before surgery. (C) After discussion with the patient, the two-stage arthroplasty strategy was selected. Thorough debridement and femoral head and neck resection were performed, and an antibiotic-impregnated cement spacer was implanted. Culture of the synovial fluid and multiple intraoperative tissues showed MSSA, which was consistent with the mNGS results (Staphylococcus). Empirical intravenous vancomycin and meropenem were administered, which was later changed to cefazolin, for a total of 3 weeks, followed by oral levofloxacin for a total of 5 weeks. (D) The second-stage revision was performed 12 weeks later. (E) At 15 months of follow-up, the function of the right hip was good, the inflammatory markers were normal, and X-ray showed satisfactory prosthesis position and no sign of infection.

**Table 2** Follow-up results of two groups of patients

	Debridement, antibiotics, and single-stage replacement (DASR)	Two-stage arthroplasty	t/z value	p value
Number	11	17	N/A	N/A
Re-admission	0	0	N/A	0.99
Re-infection	0	0	N/A	0.99
Re-revision	0	0	N/A	0.99
Dislocation	1	1	N/A	0.99
Spacer fracture	N/A	1	N/A	N/A
Aseptic loosening	0	0	N/A	0.99
DVT	0	1	N/A	0.99
Mean FU (months)	36.3 ± 15.6	37.2 ± 20.0	0.13	0.90
HHS score	83.0 ± 6.6	77.8 ± 8.2	1.80	0.08

Abbreviations: DVT, deep venous thrombosis; FU, follow-up; HHS, Harris Hip Score.

Among the five positive results, one case (Case 11) was negative in the intraoperative joint fluid and tissue cultures. The sonication fluid showed MRSE, and mNGS revealed

*S. epidermidis*, which was consistent with the results of the sonication fluid. In another case (Case 13), the culture of preoperative aspirated fluid was negative, while mNGS suggested *S. aureus*, which was consistent with the results of the intraoperative joint fluid and tissue cultures (MSSA). The culture results of these two cases with negative mNGS were also negative (Cases 1 and 14).

### Complications

In the DASR group, one patient (Case 7) was complicated with dislocation 11 days after the operation due to a fall and was managed successfully with closed reduction under anesthesia. No patients were lost to follow-up. At the last follow-up, there was no recurrence of infection. A typical case (Case 3) is shown in Figure 3. In the two-stage arthroplasty group, one patient (Case 16) was complicated with spacer fracture at 3 weeks after the first-stage surgery. The patient chose conservative treatment and underwent second-stage revision 3 months later. One patient (Case 3) was complicated with spacer dislocation after a fall and was successfully managed with closed reduction. One patient (Case 9) developed deep venous thrombosis (DVT) and was administered anticoagulation therapy. No patients were lost



to follow-up. At the last follow-up, there was no recurrence of infection. A typical case (Case 4) is shown in Figure 4. The incidences of readmission, reinfection, rerevision, dislocation, aseptic loosening, and complications were recorded at the last follow-up. The HHS score was evaluated at the last follow-up by the same personnel who evaluated the preoperative HHS score. The statistical analysis showed that there was no significant difference between the two groups in the incidences of readmission, reinfection, rerevision, dislocation, aseptic loosening, complications, or HHS at the last follow-up (Table 2).

### Discussion

SHA is a rare but difficult-to-treat disease. The incidence of PJI after primary joint replacement is 1%–2%, but it can reach 8% if there was a history of SHA in the past<sup>18</sup>. Therefore, whether patients with SHA can undergo joint replacement and how to avoid the recurrence of infection after joint replacement are the focus of surgeons.

### Main Findings

The main findings of this study were that surgery with sensitive antibiotics achieved satisfactory outcomes in the treatment of chronic destructive SHA. Both DASR and two-stage arthroplasty achieved a satisfactory infection cure rate and functional recovery for chronic destructive SHA, with no recurrence of infection seen in either group. Specifically, DASR demonstrated significantly lower intraoperative blood loss, hospital stay, and hospitalization costs than two-stage arthroplasty.

### Two-Stage Arthroplasty for Chronic Destructive SHA

The treatment of chronic destructive SHA is still not unified. In recent years, the mainstream surgical treatment has been two-stage arthroplasty. Many studies have shown satisfactory results of two-stage arthroplasty in the treatment of chronic destructive SHA<sup>2,5,10–12</sup>. However, some other studies still reported an infection recurrence rate of 0%–18%<sup>9–12,16,18–22</sup>. It is speculated that the success rate may be closely related to host nutrition and immune status, the surgical technique, microbiology, the selection of antibiotics, and the duration of treatment. Tan *et al.*<sup>16</sup> and Xu *et al.*<sup>22</sup> showed that antibiotic-resistant bacteria were an important factor leading to treatment failure. In our study, among the 17 patients who underwent two-stage revision, there was no recurrence of infection. In particular, there was one case of MRSA and three cases of MRSE, but all were successfully cured. We believe the high success rate depends on standardized surgical techniques, complete microbiology results, and sensitive antibiotics. First, thorough and radical debridement should be performed during the operation. Second, the specimen collection method must be standardized. Third, patients should discontinue antibiotics for at least 2 weeks before obtaining specimens. For cases with difficult aspiration, puncture under the guidance of ultrasound is recommended. Fourth, if implants are present, the removed hardware should be sent for sonication testing to improve the positive

rate of culture. There was one case (Case 11) in the two-stage arthroplasty group with postoperative infection of the acetabular fracture. The intraoperative joint fluid and tissue cultures were negative, but the sonication fluid culture was positive, indicating MRSE, which was consistent with the mNGS results. In another patient (Case 16) with postoperative infection of a femoral neck fracture, the intraoperative joint fluid and tissue cultures were both negative, but the culture of the sonication fluid of the screw suggested *Streptococcus*. This study, including the previous studies of our team, adds additional evidence that sonication has potential in improving the detection rate of microorganisms<sup>23</sup>. Currently, sonication has been routinely applied to cases of implant-related infection at our institution. Last, cases with mixed infection were not found in our cohorts, which may also be one of the factors leading to successful treatment.

In addition to the recurrence of infection, aseptic loosening, dislocation, and spacer fracture have also been reported in the literature<sup>9,24</sup>. Some patients even underwent multiple spacer replacements before the second-stage revision<sup>1,5,22</sup>. In our 17 cases, one case of spacer fracture and one case of spacer dislocation were also noted. Spacer fracture occurred in the early years when we used a single Steiner needle as the “backbone” of the spacer. It is speculated that the strength of this type of spacer is limited and cannot resist excessive stress and shear force. Currently, a spacer of the cemented stem is routinely used in our two-stage protocol<sup>25</sup>.

### DASR for Chronic Active SHA

However, there are few reports on whether single-stage replacement can be used in patients with active SHA. Throughout the literature, most of the reports were published in the last century, showing that one-stage replacement has good results for SHA in the quiescent stage but poor results for SHA in the active stage<sup>9</sup>. In a recent study that included 105 cases of conversion THA for SHA, I&D in the first stage followed by elective arthroplasty in the second stage was performed. The incidence of PJI was 12.4%<sup>16</sup>. In our cohort, we performed DASR in 11 cases with chronic active SHA, and the mid-term follow-up results showed that all the infections were eradicated. There was no significant difference in the incidences of readmission, rerevision, dislocation, aseptic loosening, complications, or HHS at the last follow-up compared to two-stage arthroplasty. In addition to a high infection eradication rate, our data also favored single-stage replacement, as it demonstrated significantly lower intraoperative blood loss, hospital stay, and hospitalization expenses.

Traditionally, active SHA has been considered a contradiction for primary hip replacement. However, our study suggests that one-stage replacement on the basis of thorough debridement and sensitive antibiotics can be a treatment option for active SHA. It is not uncommon in clinical practice that some patients have chronic active SHA but are not correctly diagnosed before surgery and receive conventional primary hip replacements. In these patients, thorough

debridement might not be performed, and a sufficient number of specimens are not collected to detect pathogens by multiple techniques to guide the selection of antibiotics. There is a possibility that these patients may encounter a high failure rate. In our practice, for each suspected case of SHA, we strictly followed the standardized protocols to confirm the diagnosis. We believe that to achieve a high success rate in the treatment of SHA with either a single-stage or two-stage protocol, reliable microbial data and standardized surgical techniques are key. First, aspiration before operation should be routinely performed, and the pus should be sent for a set of examinations but not limited to conventional culture. It should be noted that in all 11 DASR cases, microbial data were available before surgery. Second, during surgery, thorough and radical debridement of all infected and potentially infected tissues and removal of infected implants and associated foreign material should be carefully performed. As mentioned, sonication of removed implants would assist in improving the detection rate of pathogens. Afterward, copious amounts of saline irrigation are required to dilute the bacterial load. Surgical instruments, gloves, and gowns should be replaced, and redraping should be performed before a new implant is inserted. A second radical debridement should be performed thereafter to remove any remnant infective tissues. Meticulous debridement is the basis for success, and we recommend that the procedure be performed by experienced surgeons who have much experience in both single-stage and two-stage revision of PJI. Third, the selection of sensitive antibiotics and the duration of treatment should be decided after consultation and discussion with infectious disease specialists.

#### **mNGS Aids in the Identification of Pathogens**

Obtaining microbial data is the key for the treatment of bone and joint infections, but the low positive rate of traditional microbial culture is still a concern. In recent years, with the development of molecular diagnostic technology, mNGS has also been widely used in the diagnosis of infectious diseases<sup>26</sup>. Previous studies by our team have shown that mNGS can not only significantly improve the pathogenic detection rate of bone and joint infection<sup>27,28</sup> but can also be used to guide the special culture method of intraoperative specimens when the routine culture is negative or the bacteriology is not available<sup>29</sup>. In this study, six patients in the DASR group were tested with mNGS, of which four patients showed completely consistent results with the culture (micromonomas, *E. coli*, *C. albicans* and *Salmonella*). One patient had a negative culture, but mNGS showed *Staphylococcus*. In the two-stage arthroplasty group, one patient had negative intraoperative joint fluid and tissue cultures, but mNGS suggested a *S. epidermidis* infection, which was consistent with the culture results of the sonication fluid. Another case had a negative culture of the preoperatively aspirated fluid, but mNGS suggested a *S. aureus* infection, which was consistent with the results of the intraoperative culture (MSSA). These data suggest that mNGS has high diagnostic accuracy, which can help to identify pathogens and guide

treatment as soon as possible before surgery. At present, in our institution, mNGS has been routinely applied to detect pathogens causing bone and joint infections.

#### **Limitations**

This study has several limitations that need to be acknowledged. First, due to the low prevalence of the disease, the number of cases involved in this research is relatively small, and the homogeneity within the group and the control of variables between the two groups are impacted, such as whether the case was suffering from primary SHA or postoperative infection or whether the case had preoperative treatments. However, SHA is an uncommon problem, and we believe that, although we have a small cohort, it is one of the largest to date in the literature and provides valuable information on an innovative treatment for this unique problem. Second, the average follow-up time of our cohorts was not long. As infection can occur or relapse at any stage after joint replacement, more time is needed to observe whether the infection has been completely eradicated. In future work, studies with better homogeneity and large sample sizes or high-quality multicenter studies are warranted.

#### **Conclusions**

We conclude that surgery with sensitive antibiotics achieved satisfactory outcomes in the treatment of chronic destructive SHA. Both DASR and two-stage arthroplasty achieved satisfactory infection cure rates and functional recovery for chronic destructive SHA, and DASR demonstrated significantly lower intraoperative blood loss, hospital stay, and hospitalization costs than two-stage arthroplasty. For appropriately indicated patients, if microbial data are available and a standardized debridement protocol is strictly followed, DASR can be an option.

#### **Author Contributions**

Chao-fan Zhang: collection and assembly of data; data analysis and interpretation; manuscript writing; Xin-yu Fang: collection and assembly of data; data analysis and interpretation; Zi-da Huang: data analysis and interpretation; Guochang Bai: data analysis and interpretation; Ze-yu Zhang: data analysis and interpretation; Ye Yang: data analysis and interpretation; Zi-jie Zhang: data analysis and interpretation; Wen-bo Li: data analysis and interpretation; Wen-ming Zhang: conception and design; data analysis and interpretation; revision of the manuscript.

#### **Conflicts of Interest**

None.

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### Authorship Declaration

The authors declare: (i) that all authors listed meet the authorship criteria according to the latest guidelines of the International Committee of Medical Journal Editors, and (ii) that all authors are in agreement with the manuscript.

### Supporting Information

Additional Supporting Information may be found in the online version of this article on the publisher's web-site:

**Supplemental Table 1.** Demographics of 11 patients receiving debridement, antibiotics, and single-stage replacement (DASR) for chronic destructive SHA.

**Supplemental Table 2.** Demographics of 17 patients receiving two-stage exchange arthroplasty for chronic destructive SHA.

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